## REMARKS

Applicants respectfully request that this application be reconsidered in view of the above amendments and the following remarks.

1. Status of the Claims

Claims 41-56 are currently pending in this application. Of these pending claims, Claims 42, 44-46, 50 and 51 have been withdrawn from further consideration by the Examiner as being drawn to non-elected species. In the above amendments, Claims 47, 48, 52 and 56 are being cancelled and Claims 57 and 58 are being added. Accordingly, upon entry of the above amendments, Claims 41, 43, 49, 53-55, 57 and 58 will be pending in this application for examination on the merits.

2. Summary of the Amendments

On page 1, the specification has been amended to incorporate a specific reference to related U.S. Application Serial No. 09/317,198, filed May 24, 1999. The instant application now claims priority to this application under 35 U.S.C. §120 as a continuation-in-part.

On page 162, the abstract has been amended to correct various obvious and inadvertent typographical errors. Additionally, the abstract has been shortened to comply with 37 C.F.R. §1.72(b) and is now one paragraph.

Claim 41 has been amended to incorporate the definition of the linker, X′, found in dependent Claim 52. Applicants note that the variables "X", "Z" "R" and "m" in the definition of the linker have been changed to "X′", "$Z^a$", "R′" and "m′" to avoid confusion with other variables used in the claims.

Claim 41 has also been amended to define the point of attachment of the L″ moiety to the linker, i.e., that L″ is attached to the linker at a position selected from the group consisting of the carboxy terminus, the amino terminus, the dihydroxyphenyl ring, the saccharide amino group and the aglycone hydroxy terminus. Support for this amendment is found, for example,

on page 38, line 10 to page 39, line 13; and Figure 9 of the application as originally filed.

Additionally, L′ has been amended to read "a moiety" in place of "a β-lactam antibiotic moiety" since such language is unnecessary in view of the chemical structures employed in Claim 41. Finally, Claim 41 has also been amended at various locations to provide language consistent with the above changes.

Claim 43 has been amended to more clearly define and distinctly claim the subject matter Applicants regard as their invention. Specifically, the term "β-lactam" has been deleted as unnecessary; the phrase "a linker" has been changed to "the linker"; and the phrase "one of $R^{18}$ and $R^{19}$ is hydrogen or alkyl" has been reworded to read "$R^{18}$ and $R^{19}$ are hydrogen or alkyl" since the subsequent proviso further indicates that $R^{18}$ or $R^{19}$ can also be a covalent bond linking the L′ moiety to the linker. Additionally, Claim 43 has been amended to correct an obvious and inadvertent error, i.e., the definition of $R^{33}$ has been corrected to read "alkylene" rather than "alkyl". This change corrects an obvious error since otherwise there is no point of attachment for the substituent containing $R^{33}$. This correction is clearly supported by the $R_2$ substituent shown for Cefepime in Figure 6B-2 and thus, one skilled in the art would clearly recognize the original definition of $R^{33}$ as an obvious error.

Claim 49 has been amended to delete the vancomycin structure and to recite in place thereof that the vancomycin moiety "is attached to the linker at the saccaride amino group of the vancomycin moiety". Support for this amendment is found, for example, on page 38, lines 11-12. Claim 49 has also been amended to depend from Claim 41 instead of now cancelled Claim 48.

Claim 53 has been amended to incorporate the definition of the linker, X′, found in dependent Claim 52. Additionally, Claim 53 been amended to define the point of attachment of the L″ moiety to the linker, i.e., that L″ is attached to the linker at a position selected from the group consisting of the carboxy terminus, the amino terminus, the dihydroxyphenyl ring and the saccharide amino group of the vancomycin moiety. Support for this amendment is found, for example, on page 38, line 10 to page 39, line 13; and Figure 9.

Claim 55 has been amended to recite "a therapeutically" effective amount. Support for this amendment is found, for example, on page 37, lines 14-19.

Additionally, Claims 57 and 58 have been added. Support for these claims is found, for example, on page 38, line 18 to page 39, line 13; page 52, line 6 to page 55, line 1 (in particular, page 54, lines 15-20); and page 56, line 16 to page 57, line 18 of the application as originally filed.

Pursuant to 37 C.F.R. §1.121, a marked-up version showing the changes made to the specification and claims is attached.

Entry of these amendments is respectfully requested.

3. Election/Restriction

Applicants hereby acknowledge that the Examiner has made final the requirement for restriction of Groups I and II. Applicants also acknowledge that Claims 42, 44-46, 50 and 51 have been withdrawn from further consideration by the Examiner pursuant to 37 C.F.R. §1.142(b) as being drawn to non-elected species. If generic Claim 41 (or another generic claim) is allowed, Applicants respectfully request reconsideration of these additional species as provided by 37 C.F.R. §1.141.

4. Information Disclosure Statement

The Examiner has indicated that the Information Disclosure Statement filed on September 13, 2000, failed to fully comply with 37 C.F.R. §1.98(a)(3) because it did not include a concise explanation of the relevance of EP 322 810 A2, a non-English language document. In response, Applicants provide the following concise explanation of EP 322 810 A2:

EP 322 810 A2 discloses 3-[(quinolonecarbonyl)thiomethyl]cephalosporins and analogs thereof, and methods for preparing such compounds. The disclosed compounds are reported to be useful as antibiotics.

Additionally, Applicants are enclosing a copy of AU-A-27554/88, which is an English language equivalent of EP 322 810 A2. Applicants respectfully request that the Examiner consider EP 322 810 A2 and initial the enclosed copy of the Form 1449 which was originally submitted with this document.

5. Objection to the Specification

The abstract of the disclosure has been objected to because it consists of two paragraphs. In response, Applicants have amended the abstract to now consist of one paragraph. Additionally, Applicants have shortened the abstract to comply with 37 C.F.R. §1.72(b). Accordingly, withdrawal of this rejection is respectfully requested.

6. Rejections Under 37 C.F.R. §112, First Paragraph

The Examiner has indicated that there are allegedly two separate issues under 35 U.S.C. §112, first paragraph, i.e., issues pertaining to the linker structure and issues pertaining to the glycopeptide antibiotic. For convenience and clarity, Applicants will respond to each of these issues separately.

A. §112 First Paragraph Issues Related to Linker Structure

Claims 41, 43, 47-49 and 53-55 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. Specifically, the Examiner has indicated that there is "a virtually unlimited number of compounds that would fall

within the claimed genus of compounds...because the instant claims give *no structure* of the linker moiety (X)" (emphasis in original). Additionally, the Examiner has stated that the instant description discloses only a limited number of examples of how the instant ligands can be linked together. The Examiner has indicated that this is a written description rejection. Applicants respectfully traverse this rejection for the following reasons.

First, Applicants have amended the pending claims to recite a specific generic formula for the linker moiety and therefore, there is no longer an infinite number of compounds encompassed by the instant claims. Each pending claim now recites a linker structure and a specific point of attachment of the linker to the ligands.

Additionally, with regard to adequate written description, Applicants respectfully point out that the instant specification, as originally filed, provides at least sixty-seven (67) specific examples of linking moieties on pages 60-65; and over four-hundred (>400) specific examples of difunctional starting materials on pages 104-109 which can be used to prepare the dimeric compounds of the present invention. Applicants respectfully submit that this extensive disclosure of specific linker moieties in combination with the general and specific synthetic methods taught in the application provides a more than adequate written description of the now claimed subject matter. Accordingly, Applicants respectfully request that this written description aspect of the rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

Claims 41, 43, 47-49 and 53-55 have also been rejected under 35 U.S.C. §112, first paragraph, because the specification, "while being enabling for specific compounds where structures of the linker moiety are shown, does not provide enablement for any compound utilizing the claimed ligands linked with *any* linker" (emphasis in original). The Examiner has also explained why she believes any necessary experimentation would be "undue" when no structural limitations are given for the linker. The Examiner has indicated that this is an enablement rejection. For the following reasons, Applicants believe that this rejection has been obviated by the above amendments.

With regard to enablement, the Examiner has indicated that "[i]t is clear from

applicant's specification how one might practice this invention with specific compounds where structures, linkage sites and linkers are shown...." (Emphasis added). As indicated above, Applicants have amended the pending claims to show specific structural formulas for each ligand and linker moiety and to further show specific points of attachment for the ligand moieties to the linker. Accordingly, Applicants respectfully submit that the present amendments have obviated this aspect of the rejection under 35 U.S.C. § 112, first paragraph.

For the foregoing reasons, Applicants respectfully request that the rejection of Claims 41, 43, 47-49 and 53-55 under 35 U.S.C. § 112, first paragraph, as applied to the linker be withdrawn.

B. §112 First Paragraph Issues Relating to the Glycopeptide Antibiotic

Claims 41, 43, 47, 48, 52, and 55 have been rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not reasonably provide enablement for any glycopeptide antibiotic other than vancomycin. For the following reasons, Applicants submit that this rejection has been obviated by the above amendments to the claims.

While not agreeing with the Examiner, in order to expedite allowance of clearly allowable subject matter, Applicants have amended Claim 41 to recite that L″ is an optionally substituted vancomycin moiety or an aglycon derivative of an optionally substituted vancomycin moiety. Similarly, Claim 53 and newly added Claim 57 recite that L″ is a vancomycin moiety. The remaining rejected claims either depend from Claims 41, 53 or 57 (i.e., Claim 55) or have been cancelled (i.e., Claims 47, 48 and 52).

Accordingly, Applicants submit that the rejection of Claims 41, 43, 47, 48, 52, and 55 under 35 U.S.C. § 112, first paragraph, as applied to the glycopeptide antibiotic has been obviated by the above amendments and therefore, withdrawal of this rejection is respectfully requested.

7. Rejections Under 37 C.F.R. §112, Second Paragraph

Claims 41, 43, 47-49 and 53-55 have been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Examiner has indicated that these claims are indefinite because they allegedly omit essential structural cooperative relationships of the elements, i.e., the structure of the linkers. For the following reasons, Applicants submit that this rejection has been obviated by the above amendments to the claims.

As discussed above, Applicants have amended all the remaining claims to recite a structural formula for the linker. In view of these amendments, Applicants submit that the rejection of Claims 41, 43, 47- 49 and 53-55 under 35 U.S.C. § 112, second paragraph, has been obviated. Accordingly, withdrawal of this rejection is respectfully requested.

8. Rejections Under 37 C.F.R. §102(e)

Claims 41, 43, 47-49 and 52-55 have been provisionally rejected under 35 U.S.C. §102(e) as allegedly being anticipated by co-pending U.S. Application Serial No. 09/317,198. For the following reasons, Applicants submit that this rejection is now moot.

First, Applicants note that the following applications, which contain subject matter related to the instant application, are pending in the United States Patent and Trademark Office:

(1) U.S. 09/317,198, filed May 24, 1999 ("the '198 application");

(2) U.S. 09/492,542, filed January 27, 2000 (a continuation of the '198 application);

(3) U.S. 09/719,066, filed December 7, 2000 (a national phase U.S. application from PCT/US99/12776, filed June 7, 1999, and corresponding essentially to the '198 application)

(4) U.S. 09/457,926, filed December 8, 1999 (the instant application).

Upon review of these applications, Applicants have determined that the instant application is properly a continuation-in-part (CIP) of the '198 application. Accordingly, Applicants are submitting herewith a newly executed Combined Declaration and Power of Attorney for the instant application in which the inventors claim the benefit under 35 U.S.C. §120 of U.S. Application Serial No. 09/317,198, filed May 24, 1999. In view of this new claim of priority for the instant application, Applicants are filing requests on even date herewith to expressly abandon the '198, '542 and '066 applications (copies of these requests for express abandonment are enclosed herewith). Accordingly, in view of the abandonment of these applications, the provisional rejection of Claims 41, 43, 47-49 and 52-55 under 35 U.S.C. §102(e) may be withdrawn.

9. Rejections Under 37 C.F.R. §§102(f) and (g)

Claims 49 and 55 have been rejected under 35 U.S.C. §102(f) because Applicants allegedly did not invent the claimed subject matter. Specifically, the Examiner has indicated that Claims 49 and 55 are directed to the same subject matter as Claims 50 and 55 of co-pending U.S. Serial No. 09/317,198, filed May 24, 1999. Additionally, the Examiner has indicated that the issue of priority under 35 U.S.C. §102(g) and possible 35 U.S.C. §102(f) for this single invention must be resolved. For the following reasons, these rejections are respectfully traversed.

To address the issues raised by the Examiner, the appropriate inventorship for the claimed subject matter in the instant application and the '198 parent application must first be understood. After careful review, it has now been determined that the correct inventorship for the '198 parent application as filed is Burton G. Christensen, Edmund J. Moran, John H. Griffin, J. Kevin Judice, YongQi Mu and John L. Pace, and that the correct inventorship for the instant application as filed (and as currently pending) is Burton G. Christensen, Edmund J. Moran, John H. Griffin, J. Kevin Judice, YongQi Mu, John L. Pace, Mathai Mammen and James Aggen – inventors Mammen and Aggen being added by virtue of their inventive

contribution to some of the new subject matter present in the instant application relative to the '198 application.

Specifically, inventor Aggen is believed to have made an inventive contribution, for example, to the L' moiety defined by structure (xvii) in instant Claim 43 and to the L' moiety defined in Claim 53; and inventor Mammen is believed to have made an inventive contribution, for example, to the L' moiety defined by structure (xi) in Claim 43. Inventors Aggen and Mammen are not believed to have made an inventive contribution to any of the claimed subject matter in the '198 parent application.

Thus, with regard to Claim 49 in the instant application and Claim 50 in the '198 application, inventorship of this subject matter is believed to be the same inventive entity in each application, i.e., Christensen, Moran, Griffin, Judice, Mu and Pace. Accordingly, since this subject matter has the same inventive entity in both applications, there can be no issue of priority of invention under 35 U.S.C. §102(g) or derivation under 35 U.S.C. §102(f) for this subject matter.

For Claim 55 in each application, Applicants first respectfully point out that these claims are not directed to exactly the same invention as indicated by the Examiner. Specifically, both these claims are directed to pharmaceutical compositions comprising a pharmaceutically acceptable carrier and an effective amount of a compound defined by the compound claims in each application. However, since the compound claims in each application are different in scope, Claim 55 in the instant application does not claim exactly the same subject matter as Claim 55 in the '198 application. In any event, as discussed above, to the extent that Claim 55 in the instant application is directed to the same subject matter as Claim 55 in the '198 application, inventorship of this subject matter is believed to be the same in each application, i.e., Christensen, Moran, Griffin, Judice, Mu and Pace. Therefore, there can be no issue of priority of invention under 35 U.S.C. §102(g) or derivation under 35 U.S.C. §102(f) for this subject matter.

Accordingly, in view of the above, Applicants respectfully request that the rejections of

Claims 49 and 55 under 35 U.S.C. §102(f) and/or 35 U.S.C. §102(g) be withdrawn.

10. Rejections Under 37 C.F.R. §103

Claims 41, 43, 47-49 and 52-55 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 5,693,791, issued to Truett, in view of Boeckh et al., *Antimicrob. Agents Chemother.*, **1988**, Vol. 32, No. 1, pp. 92-95. For the following reasons, this rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, three requirements must be satisfied. First, the prior art relied upon, coupled with the knowledge generally available in the art at the time of the invention, must contain some suggestion or incentive that would have motivated the skilled artisan to modify the references or to combine the references in a manner that produces the claimed invention. See, *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988). Second, the proposed modification of the prior art must have had a reasonable expectation of success as determined from the vantage point of the skilled artisan at the time the invention was made. See, *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1209, 18 U.S.P.Q.2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art reference or combination of references must teach or suggest all the limitations of the claims. See, *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970). The above teachings or suggestions, as well as the expectation of success, must come from the prior art, not from applicant's own disclosure. See, *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991).

In the present case, the Examiner has indicated that the Truett reference teaches the linking of diverse antibiotic moieties to form dimers; and that the Boeckh reference teaches combination therapy using vancomycin and ceftazidime. Accordingly, the Examiner has concluded that it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to link vancomycin and ceftazidime to create a broad spectrum antibiotic compound. For the following reasons, Applicants respectfully disagree with this conclusion.

First, the pending claims in this application are now directed to chemical compounds (and pharmaceutical compositions containing such compounds) having a specified chemical structure which includes specific points of attachment for each component. In this regard, the cited references clearly provide no motivation or suggestion to make the specific chemical compounds of the instant claims. Specifically, the Truett reference lacks the disclosure of any glycopeptide antibiotic and thus fails to provide any motivation to link glycopeptide antibiotics to β-lactam antibiotics.

In particular, Applicants note that the Truett reference itself explicitly states the types of antibiotics that can linked together (in Column 6, lines 34-38) as follows:

> "*The types of antibiotics that can be linked are* sulfonamides, trimethoprim, penicillins and related structures, cephalosporins and related structures, chloramphicol, erythromycin, metronidiazole, quinolones, tetracyclines and aminoglycosides." (emphasis added).

Noticeably absent from this list are glycopeptide antibiotics which were well-known at the time the Truett application was filed (i.e., April 11, 1995). When determining whether a reference provides motivation for a particular course of action, one cannot ignore the explicit teachings of the reference itself. Here, the Truett reference explictly states the types of antibiotics that can be linked together and that list does not include glycopeptide antibiotics.

The secondary reference, Boeckh et al., merely discloses physical mixtures of vancomycin and ceftazidime. Since it is solely concerned with physical mixtures of such compounds, this reference does not provide any motivation to link such compounds together.

Even more apparent is the fact that the cited references, either alone or in combination, fail to provide any suggestion, motivation or guidance on how to specifically link glycopeptide and β-lactam antibiotics to arrive at Applicants' specific chemical structures. In this regard, Applicants further note the there is no structural similarity between any of the chemical structures

disclosed in the cited references and Applicants' present claimed compounds. Thus, there is clearly no motivation to make any of the specific molecular modifications necessary to arrive at the presently claimed invention. Accordingly, Applicants respectfully submit that the cited references do not provide the requisite motivation necessary to establish a *prima facie* case of obviousness for the now claimed subject matter.

Second, it was well-known in the art at the time the present invention was made that structural modifications of biologically active compounds affect the biological activity or efficacy of such compounds – this being the fundamental basis for the science of medicinal chemistry. In the present case, the structural modifications being suggested by the Examiner significantly change the chemical structure of both the glycopeptide antibiotic and the β-lactam antibiotic. Accordingly, Applicants respectfully submit that one skilled in the art could not have predicted *a priori* whether a covalently-linked glycopeptide – β-lactam dimer would have antibacterial activity because such chemical modifications are outside the scope of the traditional structure/activity relationships understood by those skilled in the art for these classes of antibiotics. Applicants acknowledge that glycopeptide dimers are known in the art to retain antibacterial activity – but such dimers are known to mimic the naturally-occurring *in situ* association of glycopeptide antibiotics (see, for example, the first paragraphs of Sundram et al., *J. Am. Chem. Soc.* **1996**, *118*, 13107 and Rao et al., *J. Am. Chem. Soc.* **1997**, *119*, 10286-10290, which were cited but not relied upon by the Examiner). There is nothing in the prior art of record that suggests that a glycopeptide modified with a β-lactam would retain its antibacterial activity or alternatively, that a β-lactam modified with a glycopeptide antibiotic would retain its antibacterial activity. Accordingly, one skilled in the art would not have had a reasonable expectation that modifying the cited references as suggested by the Examiner would succeed in producing a compound having antibacterial properties. At best, such modifications might be deemed "obvious to try" or an "invitation to experiment" but, as the Examiner is well aware, obvious to try is not the appropriate standard for determining *prima facie* obviousness.

Finally, Applicants note that the cited references, either alone or in combination with

each other, do not teach or suggest all the limitations of the presently pending claims. For example, among other limitations, the cited references fail to teach or suggest the particular points of attachment found in the presently claimed compounds.

In summary, for the foregoing reasons, Applicants respectfully submit that the cited references provide no motivation or suggestion to make the specific chemical compounds of the instant claims. Additionally, one skilled in the art would not have had a reasonable expectation that combining the references in the manner suggested by the Examiner would succeed in producing compounds having antibiotic properties. Moreover, even if the references are combined in the manner suggested by the Examiner, the resulting combination does not teach or suggest each and every limitation of the presently claimed subject matter. Thus, the cited references fail to establish a *prima facie* case of obviousness for the presently claimed subject matter. Accordingly, Applicants respectfully request that the rejection of Claims 41, 43, 47-49 and 52-55 under 35 U.S.C. §103(a) be withdrawn.

11. Double Patenting Rejection Under 35 U.S.C. §101

Claims 49 and 55 have been provisionally rejected under 35 U.S.C. §101 as allegedly claiming the same invention as that of Claims 50 and 55 in commonly-assigned copending U.S. Application Serial No. 09/317,198. This provisional rejection is now moot in view of the express abandonment of the '198 application. Therefore, withdrawal of this rejection is respectfully requested.

12. Obviousness-type Double Patenting Rejection

Claims 41, 43, 47, 48 and 52-54 have been provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 43-49, 53, 54 and 57-61 of copending U.S. Application No. 09/317,198. This provisional rejection is also now moot in view of the express abandonment of the '198 application. Accordingly, Applicants respectfully request that this provisional rejection be withdrawn.

13. Petition to Correct Inventorship

In reviewing the inventorship of this application, it has been determined that John L. Pace was inadvertently omitted as an inventor without any deceptive intention. Accordingly, Applicants are submitting herewith a petition under 37 C.F.R. §1.48(a) to add inventor Pace to the instant application. This petition is accompanied by (a) a statement from inventor Pace that the error in inventorship occurred without deceptive intention on his part; (b) a newly executed declaration by the actual inventors; (c) the processing fee set forth in §1.17(i); and (d) the written consent of the assignee.

As discussed above, it has also been determined that inventorship of the '198 parent application was inadvertently incorrect as originally filed. However, since this application is being expressly abandoned, Applicants believe that correction of the inventorship in this application is not necessary. Accordingly, no new papers relating to inventorship of the '198 application are being submitted.

For the foregoing reasons, Applicants believe that this application is now in condition for allowance. Should there be any remaining issues that can be resolved by telephone, the Examiner is respectfully requested to telephone the undersigned attorney at (650) 808-6406.

Respectfully submitted,

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## VERSION OF AMENDMENTS WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

The abstract on page 162 has been amended as follows:

This invention relates to novel multibinding compounds (agents) that are antibacterial agents. The multibinding compounds of the invention comprise from 2-10 ligands covalently connected by a linker or linkers, wherein each of said ligands in their monovalent (i.e., unlinked ) state [have] has the ability to bind to [a] an enzyme involved in cell wall biosynthesis and metabolism, a precursor used in the synthesis of the bacterial cell wall and/or the bacterial cell surface thereby [interfere] interfering with the synthesis and/or metabolism of the cell wall. [In particular the multibinding compounds of the invention comprise from 2-10 ligands covalently connected by a linker or linkers, wherein each of said ligands has[

]a ligand domain capable of binding to penicillin binding proteins, a transpeptidase enzyme, a substrate of a transpeptidase enzyme, a beta-lactamase enzyme, pencillinase enzyme, cephalosporinase enzyme, a transglycoslase enzyme, or a transglycosylase enzyme substrate;] Preferably, the ligands are selected from the beta-lactam or glycopeptide class of antibacterial agents.

In the Claims:

Please cancel Claims 47, 48, 52 and 56 without prejudice or disclaimer.

Please amend Claim 41 as follows:

41. (Amended) A compound of the formula:

[L′-X-L″] L′-X′-L″

[wherein X is a linker;

L′ is a β-lactam antibiotic moiety; and

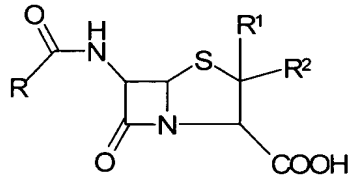
L″ is an optionally substituted glycopeptide antibiotic moiety or an aglycon derivative of an optionally substituted glycopeptide antibiotic moiety;

and further wherein the β-lactam antibiotic]

or a pharmacetically acceptable salt thereof; wherein

L′ is a moiety is selected from the group consisting of:

(i) a moiety of formula (a):



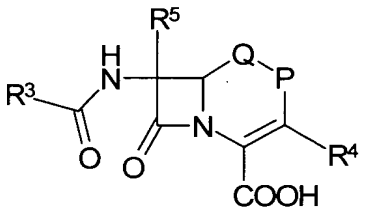

(a)

wherein:

R is selected from the group consisting of substituted alkyl, aryl, aralkyl, and heteroaryl wherein each of said substituents optionally links (a) to the linker via a covalent bond or R is a covalent bond that links (a) to the linker; and

$R^1$ and $R^2$ are, independently of each other, alkyl or at least one of $R^1$ or $R^2$ is a covalent bond linking (a) to the linker provided that only one of R, $R^1$ or $R^2$ links said moiety to said linker;

(ii) a moiety of formula (b):




(b)

wherein:

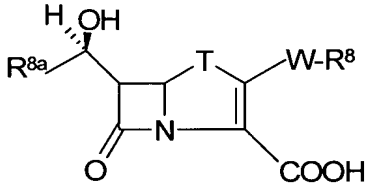
one of P and Q is O, S, or $-CH_2-$ and the other is $-CH_2-$;

$R^3$ is selected from the group consisting of substituted alkyl, heteroarylalkyl, aralkyl, heterocyclylalkyl, and $-C(R^6)=NOR^7$, wherein $R^6$ is aryl, heteroaryl, or substituted alkyl and $R^7$ is alkyl or substituted alkyl and further wherein each of said substituents optionally links (b) to the linker via a covalent bond or $R^3$ is a covalent bond that links (b) to the linker; and

$R^4$ is selected from the group consisting of hydrogen, alkyl, alkenyl, substituted alkenyl, substituted alkyl, halo, heteroarylalkyl, heterocyclylalkyl, $-SR^a$ and $-CH_2SR^a$, where $R^a$ is aryl, heteroaryl, heterocyclyl or cycloalkyl wherein each of said substituents optionally links (b) to the linker or $R^4$ is a covalent bond that links (b) to the linker provided that only one of said $R^3$ substituents or covalent bond and $R^4$ substituents or covalent bond links said moiety to said linker; and

$R^5$ is selected from the group consisting of hydrogen, hydroxy, and alkoxy;

(iii) a moiety of formula (c):




(c)

wherein:

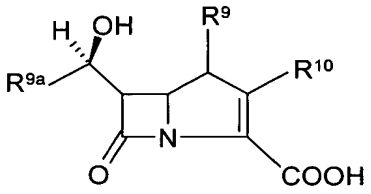
T is S or $CH_2$,

$R^{8a}$ is alkyl;

W is selected from the group consisting of O, S, $-OCH_2-$, and $CH_2$; and

$R^8$ is -(alkylene)-$NHC(R^b)=NH$ where $R^b$ is a covalent bond that links (c) to the linker; or $-W-R^8$ is a covalent bond that links (c) to the linker provided that only one of $R^b$ or $-W-R^8$ binds said moiety to said linker;

(iv) a moiety of formula (d):




(d)

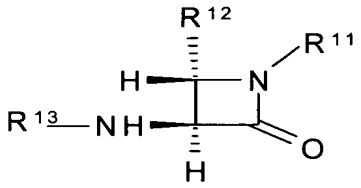
wherein:

$R^9$ and $R^{9a}$ are alkyl;

$R^{10}$ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, halo, aryl, heteroaryl, heterocyclyl, aralkyl, heteroaralkyl, heterocyclylalkyl and $-CH_2SR^a$, where $R^a$ is aryl, heteroaryl, heterocyclyl or cycloalkyl wherein each of said substituents optionally links (d) to the linker or at least one of $R^9$ and $R^{10}$ is a covalent bond that links (d) to the linker; or

$R^9$ and $R^{10}$, together with the carbon atoms to which they are attached, form an aryl, heteroaryl, cycloalkyl, substituted cycloalkyl, or heterocyclyl ring of from 4 to 7 ring atoms wherein one of the ring atoms optionally links (d) to the linker provided that only one of said substituents, ring atoms, $R^9$ or $R^{10}$ links said moiety to said linker; and

(v) a moiety of formula (e):




(e)

wherein:

$R^{11}$ is selected from the group consisting of $-SO_3H$ or -(alkylene)-COOH;

$R^{12}$ is selected from the group consisting of alkyl, substituted alkyl, haloalkyl, alkoxy, aryl, aralkyl, heteroaryl, heteroaralkyl, cycloalkyl, substituted cycloalkyl, and heterocyclyl wherein each of said substituents optionally binds (e) to the linker or $R^{12}$ is a covalent bond that links (e) to the linker;

$R^{13}$ is selected from the group consisting of alkyl, acyl, or $-COC(R^{14})=N-OR^{15}$ wherein

$R^{14}$ is aryl or heteroaryl which optionally links (e) to the linker, and $R^{15}$ is -(alkylene)-$COOR^{16}$ wherein $R^{16}$ is hydrogen or a covalent bond that optionally links (e) to the linker or $R^{13}$ is a covalent bond that links (e) to the linker provided that only one of $R^{12}$, $R^{13}$, $R^{14}$ or $R^{15}$ links said moiety to said linker;

L″ is an optionally substituted vancomycin moiety or an aglycon derivative of an optionally substituted vancomycin moiety, wherein L″ is attached to the linker at a position selected from the group consisting of the carboxy terminus, the amino terminus, the dihydroxyphenyl ring, the vancosamine amino group and the aglycone hydroxy terminus;

X′ is a linker of the formula:

$$-X^a-Z^a-(Y^a-Z^a)_{m'}-X^a-$$

wherein

*m*' is an integer of from 0 to 20;

$X^a$ at each separate occurrence is selected from the group consisting of -O-, -S-, -NR′-, -C(O)-, -C(O)O-, -OC(O)-, -C(O)NR′-, -NR′C(O)-, C(S), -C(S)O-, -C(S)NR′-, -NR′C(S)-, and a covalent bond;

$Z^a$ at each separate occurrence is selected from the group consisting of alkylene, substituted alkylene, cycloalkylene, substituted cylcoalkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, cycloalkenylene, substituted cycloalkenylene, arylene, heteroarylene, heterocyclene, and a covalent bond;

each $Y^a$ at each separate occurrence is selected from the group consisting of -O-, -C(O)-, -OC(O)-, -C(O)O-, -NR′-, -S(O)n-, -C(O)NR′-, -NR′C(O)-, -NR′C(O)NR′-, -NR′C(S)NR′-, -C(=NR′)-NR′-, -NR′-C(=NR′)-, -OC(O)-NR′-, -NR′-C(O)-O-, -P(O)(OR′)-O-, -O-P(O)(OR′)-, $-S(O)_nCR'R''-$, $-S(O)_n-NR'-$, $-NR'-S(O)_n-$, -S-S-, and a covalent bond; where *n* is 0, 1 or 2; and

R′ and R″ at each separate occurrence are selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl,

cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, aryl, heteroaryl and heterocyclic.

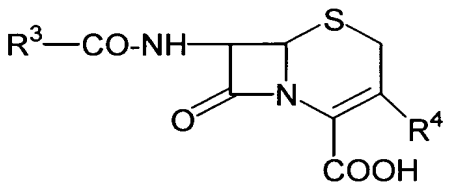
[and pharmaceutically acceptable salts thereof

[provided that when L″ is a vancomycin moiety attached via its carboxyl group to the linker, X, then the β-lactam antibiotic moiety, L′, is not a cefalexin moiety attached to the linker, X, via acylation of its α-amino group]

provided that when L″ is a vancomycin moiety attached via its carboxyl group to the linker, then L′ is not a cefalexin moiety attached to the linker via acylation of its α-amino group.

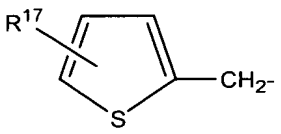
Please amend Claim 43 as follows:

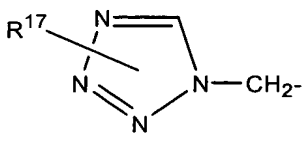
43. (Amended) The compound of Claim 41, wherein [the β-lactam moiety has] L′ is a moiety of the formula:

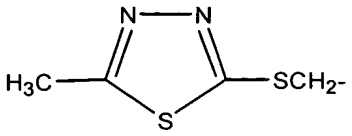


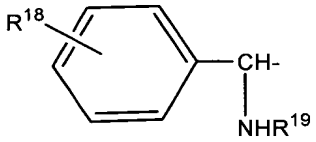

where:

$R^3$ and $R^4$ are selected from the group consisting of:

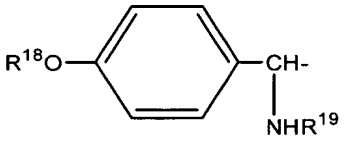
| | $R^3$ | $R^4$ |
|---|---|---|
| (i) |  | $-CH_2OCOCH_3$ |

(ii) 

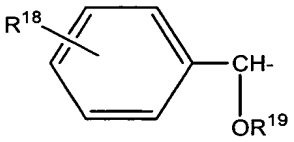


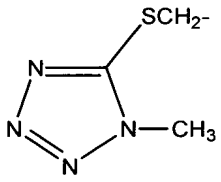
(iii) 

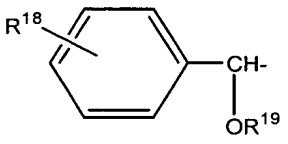
$-CH_3$

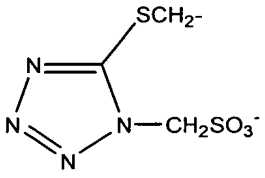
(iv) 

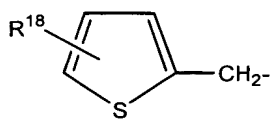
$-CH_3$

(v) 

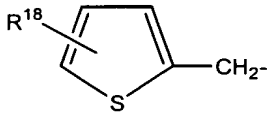


(vi) 

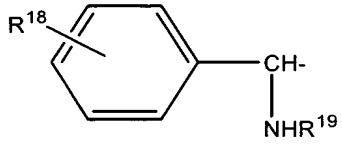


(vii) 

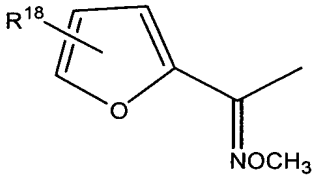

$-CH_2OCONHR^{19}$

(viii) 

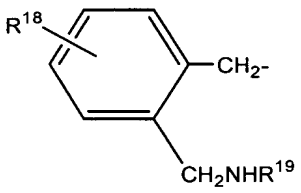

$-CH_2OCOCH_3$

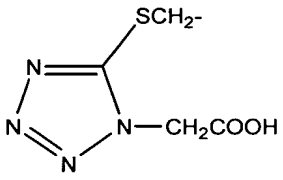
(ix) 


-Cl

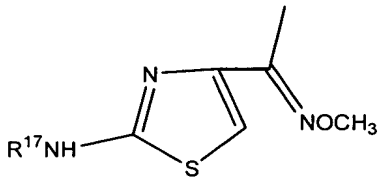
(x) 


$-CH_2OCONHR^{19}$

(xi) 

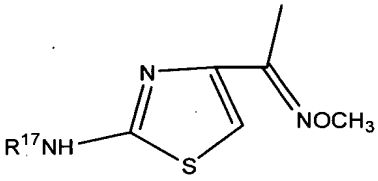



(xii)



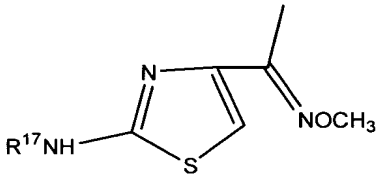

$-CH_2OCOCH_3$

(xiii)



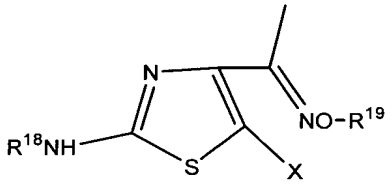

$-CH_2OCH_3$

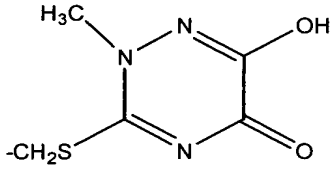
(xiv)



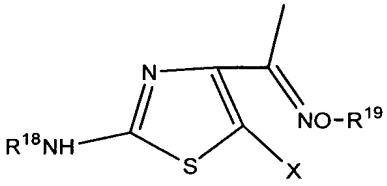

-H

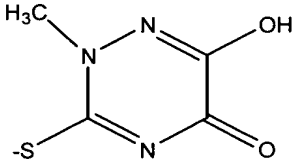
(xv)



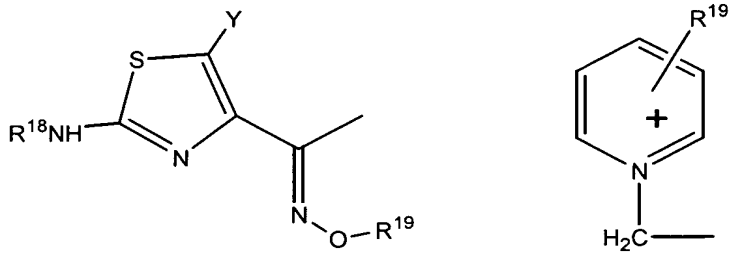




(xvi)

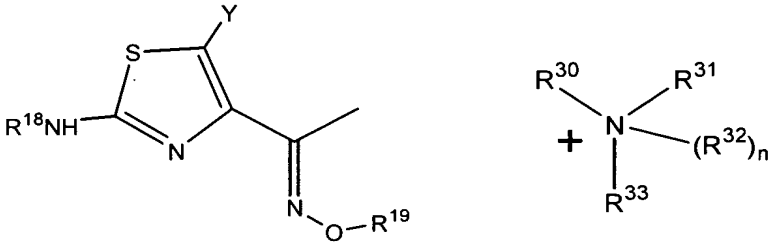


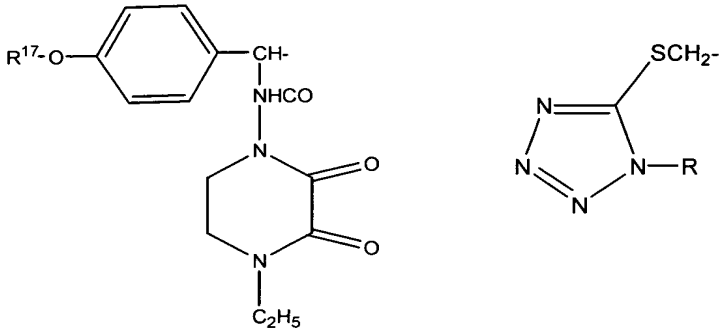
(xvii)



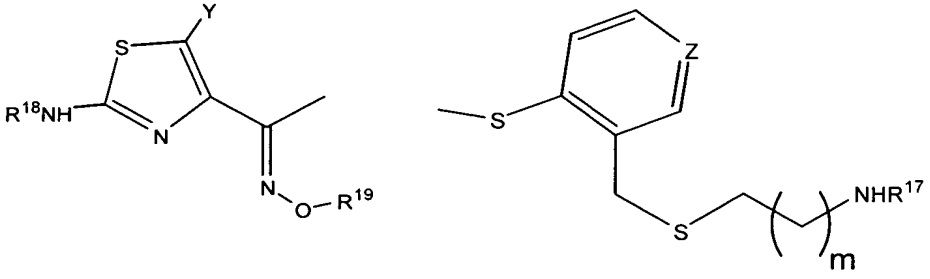
(xviii)

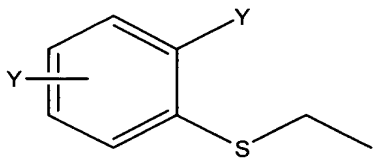
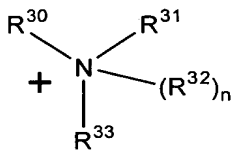


(xix)



(xx)



(xi)  

wherein:

R is alkyl;

$R^{17}$ is a covalent bond that links the [β-lactam] L′ moiety to [a] the linker;

[one of] $R^{18}$ and $R^{19}$ [is] are hydrogen or alkyl;

$R^{30}$ and $R^{31}$ are, independently of each other, hydrogen or alkyl; or together with the nitrogen atom to which they are attached form a heterocycloamino group;

$R^{32}$ [and $R^{33}$ are independently] is alkyl;

$R^{33}$ is alkylene;

X is halo;

Y is hydrogen or halo;

Z is CH or N;

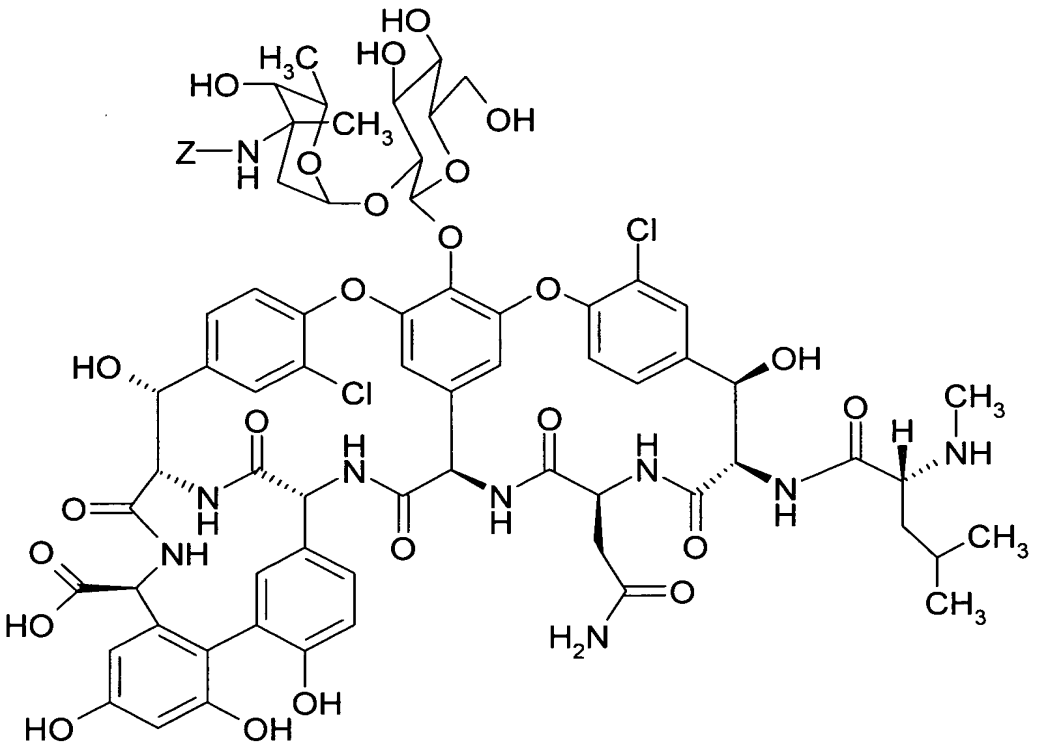
*m* is an integer from 1 to 5;

*n* is 0 or 1;

and further wherein one of $R^{18}$, $R^{19}$, $R^{30}$, $R^{31}$, $R^{32}$ and $R^{33}$ is a covalent bond that links the [β-lactam] L′ moiety to the linker.

Please amend Claim 49 as follows:

49. (Amended) The compound according to Claim [48] 41 wherein L″ is a vancomycin moiety which is attached to the linker at the saccharide amino group of the vancomycin moiety [represented by the formula:



wherein Z is the point of linkage for the vancomycin moiety to the linker moiety X].

Please amend Claim 53 as follows:

53. (Amended) A compound of the formula:

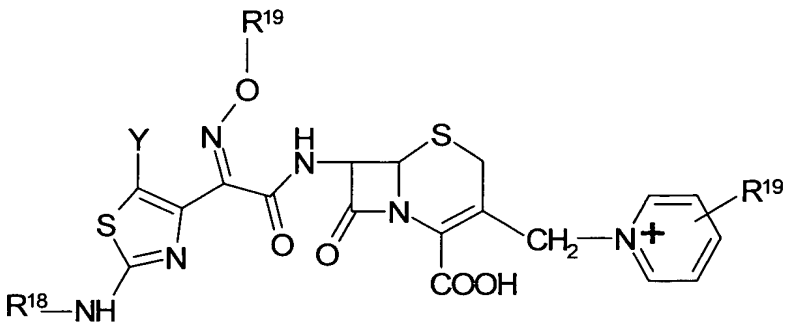
[L′-X-L″] L′-X′-L″

[wherein X is a linker;

L′ is a β-lactam antibiotic]

or pharmaceutically acceptable salts thereof; wherein

L′ is a moiety of the formula:



wherein

Y is selected from the group consisting of hydrogen and halogen;

$R^{18}$ and $R^{19}$ are selected from the group consisting of hydrogen or alkyl provided that one of $R^{18}$ and $R^{19}$ is a covalent bond which links the [β-lactam antibiotic] L′ moiety to the linker; and

L″ is a vancomycin [antibiotic] moiety, wherein L″ is attached to the linker at a position selected from the group consisting of the carboxy terminus, the amino terminus, the dihydroxyphenyl ring and the saccharide amino group of the vancomycin moiety;

X′ is a linker of the formula:

$$-X^a-Z^a-(Y^a-Z^a)_{m'}-X^a-$$

wherein

*m'* is an integer of from 0 to 20;

$X^a$ at each separate occurrence is selected from the group consisting of -O-, -S-, -NR′-, -C(O)-, -C(O)O-, -OC(O)-, -C(O)NR′-, -NR′C(O)-, C(S), -C(S)O-, -C(S)NR′-, -NR′C(S)-, and a covalent bond;

$Z^a$ at each separate occurrence is selected from the group consisting of alkylene, substituted alkylene, cycloalkylene, substituted cylcoalkylene, alkenylene, substituted alkenylene, alkynylene, substituted alkynylene, cycloalkenylene, substituted cycloalkenylene, arylene,

heteroarylene, heterocyclene, and a covalent bond;

each $Y^a$ at each separate occurrence is selected from the group consisting of -O-, -C(O)-, -OC(O)-, -C(O)O-, -NR'-, -S(O)n-, -C(O)NR'-, -NR'C(O)-, -NR'C(O)NR'-, -NR'C(S)NR'-, -C(=NR')-NR'-, -NR'-C(=NR')-, -OC(O)-NR'-, -NR'-C(O)-O-, -P(O)(OR')-O-, -O-P(O)(OR')-, $-S(O)_nCR'R''-$, $-S(O)_n-NR'-$, $-NR'-S(O)_n-$, -S-S-, and a covalent bond; where *n* is 0, 1 or 2; and

R' and R" at each separate occurrence are selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, aryl, heteroaryl and heterocyclic.

Please amend Claim 55 as follows:

55. (Amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and [an] a therapeutically effective amount of a compound of any of [Claims 41-54] Claims 41-46, 49-51, 53, 54, 57 or 58.